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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Dec 17	The CA Lexicon available in the CAPLUS and CA files
NEWS 3	Feb 06	Engineering Information Encompass files have new names
NEWS 4	Feb 16	TOXLINE no longer being updated
NEWS 5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS 6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS 7	May 07	DGENE Reload
NEWS 8	Jun 20	Published patent applications (A1) are now in USPATFULL
NEWS 9	JUL 13	New SDI alert frequency now available in Derwent's DWPI and DPCI
NEWS 10	Aug 23	In-process records and more frequent updates now in MEDLINE
NEWS 11	Aug 23	PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA
NEWS 12	Aug 23	Adis Newsletters (ADISNEWS) now available on STN
NEWS 13	Sep 17	IMSworld Pharmaceutical Company Directory name change to PHARMASEARCH
NEWS 14	Oct 09	Korean abstracts now included in Derwent World Patents Index
NEWS 15	Oct 09	Number of Derwent World Patents Index updates increased
NEWS 16	Oct 15	Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS 17	Oct 22	Over 1 million reactions added to CASREACT
NEWS 18	Oct 22	DGENE GETSIM has been improved
NEWS 19	Oct 29	AAASD no longer available
NEWS 20	Nov 19	New Search Capabilities USPATFULL and USPAT2
NEWS 21	Nov 19	TOXCENTER(SM) - new toxicology file now available on STN
NEWS 22	Nov 29	COPPERLIT now available on STN
NEWS 23	Nov 29	DWPI revisions to NTIS and US Provisional Numbers
NEWS 24	Nov 30	Files VETU and VETB to have open access
NEWS 25	Dec 10	WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS 26	Dec 10	DGENE BLAST Homology Search
NEWS 27	Dec 17	WELDASEARCH now available on STN
NEWS 28	Dec 17	STANDARDS now available on STN
NEWS 29	Dec 17	New fields for DPCI
NEWS 30	Dec 19	CAS Roles modified
NEWS 31	Dec 19	1907-1946 data and page images added to CA and CAplus

NEWS EXPRESS	August 15 CURRENT WINDOWS VERSION IS V6.0c, CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP), AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
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NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 15:38:57 ON 14 JAN 2002

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FULL ESTIMATED COST	0.60	0.60

FILE 'EMBASE' ENTERED AT 15:41:30 ON 14 JAN 2002

FILE 'BIOSIS' ENTERED AT 15:41:30 ON 14 JAN 2002

FILE 'MEDLINE' ENTERED AT 15:41:30 ON 14 JAN 2002

=> S (PEX) and (Parathyroid hormone or PTH or PTHrP)
L1 16 (PEX) AND (PARATHYROID HORMONE OR PTH OR PTHRP)

=> L1 and transgenic mammal
L1 IS NOT A RECOGNIZED COMMAND
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=> S L1 and (transgenic mammal)
L2 0 L1 AND (TRANSGENIC MAMMAL)

=> S L1 and metabolic bone disease?
L3 3 L1 AND METABOLIC BONE DISEASE?

=> S (animal model) and (PEX)
L4 28 (ANIMAL MODEL) AND (PEX)

=> Dup rem L1 L3 L4
PROCESSING COMPLETED FOR L1
PROCESSING COMPLETED FOR L3
PROCESSING COMPLETED FOR L4
L5 29 DUP REM L1 L3 L4 (18 DUPLICATES REMOVED)

=> Display L5 IBIB ABS TOTAL

L5 ANSWER 1 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002003605 EMBASE

TITLE: Simultaneous inhibition of glioma angiogenesis, cell proliferation, and invasion by a naturally occurring fragment of human metalloproteinase-2.

AUTHOR: Bello L.; Lucini V.; Carrabba G.; Giussani C.; Machluf M.; Pluderi M.; Nikas D.; Zhang J.; Tomei G.; Villani R.M.; Carroll R.S.; Bikfalvi A.; Black P.M.

CORPORATE SOURCE: R.S. Carroll, Brigham and Women's Hospital, 221 Longwood Avenue, Boston, MA 02115, United States. rcarroll@rics.bwh.harvard.edu

SOURCE: Cancer Research, (15 Dec 2001) 61/24 (8730-8736).
Refs: 40
ISSN: 0008-5472 CODEN: CNREA8

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Angiogenesis, tumor cell proliferation, and migration are the hallmarks of solid tumors, such as gliomas. This study demonstrates that a fragment derived from the autocatalytic digestion of matrix metalloproteinase (MMP)-2, called **PEX**, acts simultaneously as an inhibitor of glioma angiogenesis, cell proliferation, and migration. **PEX** is detected in the cultured medium of various human glioma, endothelial, breast, and prostate carcinoma cell lines. **PEX** is purified from the medium of glioma cell lines by chromatography, where **PEX** is constitutively expressed as a free and a TIMP-2-bound form. In human glioma tissue, **PEX** expression correlates with histological subtype and grade and with .alpha.v.beta.3 integrin expression to which it is bound. Systemic administration of **PEX** to s.c. and intracranial human glioma xenografts results in a 99% suppression of tumor growth with no signs of toxicity. Thus, **PEX** is a very promising candidate for the treatment of human malignant gliomas.

L5 ANSWER 2 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001376119 EMBASE
TITLE: Low-dose chemotherapy combined with an antiangiogenic drug reduces human glioma growth in vivo.
AUTHOR: Bello L.; Carrabba G.; Giussani C.; Lucini V.; Cerutti F.; Scaglione F.; Landre J.; Pluderi M.; Tomei G.; Villani R.; Carroll R.S.; Black P.Mc.L.; Bikfalvi A.
CORPORATE SOURCE: L. Bello, Institute of Neurosurgery, University of Milano, Ospedale Maggiore Policlinico, Via Francesco Sforza 35, 20122 Milan, Italy. lbello@rics.bwh.harvard.edu
SOURCE: Cancer Research, (15 Oct 2001) 61/20 (7501-7506).
Refs: 23
ISSN: 0008-5472 CODEN: CNREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB This study evaluates the efficacy of the combination of an antiangiogenic drug and conventional chemotherapeutics for the treatment of experimental human gliomas. As an antiangiogenic, we used recombinant human **PEX**, a fragment of matrix metalloproteinase-2 that we have previously shown to have a significant antimitotic, anti-invasive, and antiangiogenic properties against human glioblastoma in vitro and in vivo. We used carboplatin and etoposide as the two chemotherapeutic drugs routinely used in our institution (Ospedale Maggiore de Milano) for the treatment of malignant gliomas. Conventional chemotherapeutic drugs were administered at high dose or at a low and semicontinuous regimen. Combined treatment of high-dose chemotherapy and **PEX** did not produce an improvement of survival in comparison with chemotherapy alone, but it was associated with a decrease in tumor volume, vascularity, and proliferative index and an increased apoptosis. All of these animals experienced severe side effects. The longest survival was documented in animals submitted to low and semicontinuous chemotherapy and antiangiogenic treatment. This regimen was associated with no side effects, marked decrease in tumor volume, vascularity, and proliferative index, and an increased apoptosis. Our data suggest that low-dose chemotherapy in combination with **PEX** can

be successfully used against human malignant glioma in vivo.

L5 ANSWER 3 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001125880 EMBASE
TITLE: Exfoliation (pseudoexfoliation) syndrome: Toward a new understanding. Proceedings of the First International Think Tank.
AUTHOR: Ritch R.; Schlotzer-Schrehardt U.
CORPORATE SOURCE: Dr. R. Ritch, The New York Eye and Ear Infirmary, The Department of Ophthalmology, 310 East 14th Street, New York, NY 10003, United States. ritch@inx.net
SOURCE: Acta Ophthalmologica Scandinavica, (2001) 79/2 (213-217). ISSN: 1395-3907 CODEN: AOSCFV
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
012 Ophthalmology
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Exfoliation (pseudoexfoliation; **PEX**) syndrome is the single most common identifiable cause of open-angle glaucoma, however, very few investigators are engaged in basic research on this disease. To stimulate the field, the First International Think Tank on Exfoliation Syndrome was held in New York in July 1999, comprising clinicians and scientists. This report is a summary of the proceedings of this meeting.

L5 ANSWER 4 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 1
ACCESSION NUMBER: 2000390076 EMBASE
TITLE: Suppression of angiogenesis by lentiviral delivery of **PEX**, a noncatalytic fragment of matrix metalloproteinase 2.
AUTHOR: Pfeifer A.; Kessler T.; Silletti S.; Cheresh D.A.; Verma I.M.
CORPORATE SOURCE: I.M. Verma, Laboratory of Genetics, Salk Institute, 10010 North Torrey Pines Road, San Diego, CA 92037, United States. verma@salk.edu
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (24 Oct 2000) 97/22 (12227-12232).
Refs: 51
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
016 Cancer
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Modulation of the balance between pro- and antiangiogenic factors holds great promise for the treatment of a broad spectrum of human disease ranging from ischemic heart disease to cancer. This requires both the identification of angiogenic regulators and their efficient delivery to target organs. Here, we demonstrate the use of a noncatalytic fragment of matrix metalloproteinase 2 (termed **PEX**) delivered by lentiviral vectors in different angiogenesis models. Transduction of human endothelial cells with **PEX** virus suppressed endothelial invasion and formation of capillary-like structures without affecting chemotaxis in vitro. Lentiviral delivery of **PEX** blocked basic fibroblast growth factor-induced matrix metalloproteinase 2 activation and angiogenesis on chicken chorioallantoic membranes. **PEX** expression also inhibited tumor-induced angiogenesis and tumor growth in a

nude mouse model. Thus, our study shows that lentiviral vectors can deliver sufficient quantities of antiangiogenic substances to achieve therapeutic effects in vivo.

L5 ANSWER 5 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000101337 EMBASE
TITLE: Effect of age on the expression of **Pex** (Phex) in the mouse.
AUTHOR: Meyer R.A. Jr.; Young C.G.; Meyer M.H.; Garges P.L.; Price D.K.
CORPORATE SOURCE: R.A. Meyer Jr., Orthopaedic Research Laboratory, Department of Orthopaedic Surgery, Carolinas Medical Center, P.O. Box 32861, Charlotte, NC 28232-2861, United States
SOURCE: Calcified Tissue International, (2000) 66/4 (282-287). Refs: 27
ISSN: 0171-967X CODEN: CTINDZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Pex** is a newly discovered gene (also called Phex) whose mutation is the cause of X-linked hypophosphatemia. Other members of this gene family encode endopeptidases that activate or inactivate endocrine and paracrine factors. Though embryonic bone expresses mRNA for the **Pex** gene at relatively high levels, we have found **Pex** expression to be widespread in adult organs and to be poorly expressed in adult bone. This led to the hypothesis that **Pex** mRNA expression changes with age. To test this, genetically normal mice of the B6C3H hybrid strain were studied at 0 (newborn), 2, 3, 10, and 72 weeks of age. Organs known to express **Pex** were collected, and RNA was extracted from them. Following reverse transcription, cDNA was amplified by the polymerase chain reaction with primers for **Pex** and G3PDH, a housekeeping gene. The amplimers were separated by electrophoresis, blotted onto nylon membranes, and hybridized with radioactively labeled internal oligonucleotide probes. The radioactivity was quantified, and the data were analyzed as the **Pex**/G3PDH ratio. The brain samples had high levels of **Pex** mRNA expression that rose slightly with age. Calvaria, kidney, and lung samples had the highest **Pex** mRNA expression at birth. In these organs **Pex** mRNA expression fell with age to undetectable or barely detectable levels. Thymus, heart, and skeletal muscle samples had low **Pex** mRNA expression at birth that did not change with age. Some organs showed a decline in G3PDH levels with age, but **Pex** expression decreased more, leading to a reduced **Pex**/G3PDH ratio. The widespread expression of mRNA for **Pex** suggests a role beyond that of phosphate homeostasis. The high level of expression in newborn animals suggests a role in growth and development. This seems to occur in addition to its role for the endocrine regulation of phosphate homeostasis by as yet unknown humoral agents that must occur throughout life. In summary, **Pex** mRNA expression is high in brain and bone at birth. Expression remains high in brain with age but falls with age in bone, kidney, and lung.

L5 ANSWER 6 OF 29 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 2001:710 BIOSIS
DOCUMENT NUMBER: PREV200100000710
TITLE: Predicting the function and subcellular location of Caenorhabditis elegans proteins similar to Saccharomyces cerevisiae beta-oxidation enzymes.
AUTHOR(S): Gurvitz, Aner (1); Langer, Sigrid; Piskacek, Martin; Hamilton, Barbara; Ruis, Helmut; Hartig, Andreas
CORPORATE SOURCE: (1) Vienna Biocenter, Institute of Biochemistry and

Molecular Cell Biology, University of Vienna, Dr Bohrgasse 9, A-1030, Vienna: AG@abc.univie.ac.at, www.at.embnet.org/bmz/ordl.htm Austria

SOURCE: Yeast, (30 September, 2000) Vol. 17, No. 3, pp. 188-200. print.
ISSN: 0749-503X.

DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The role of peroxisomal processes in the maintenance of neurons has not been thoroughly investigated. We propose using Caenorhabditis elegans as a model organism for studying the molecular basis underlying neurodegeneration in certain human peroxisomal disorders, e.g. Zellweger syndrome, since the nematode neural network is well characterized and relatively simple in function. Here we have identified C. elegans **PEX**-5 (C34C6.6) representing the receptor for peroxisomal targeting signal type 1 (PTS1), defective in patients with such disorders. **PEX**-5 interacted strongly in a two-hybrid assay with Gal4p-SKL, and a screen using **PEX**-5 identified interaction partners that were predominantly terminated with PTS1 or its variants. A list of C. elegans proteins with similarities to well-characterized yeast beta-oxidation enzymes was compiled by homology probing. The possible subcellular localization of these orthologues was predicted using an algorithm based on trafficking signals. Examining the C termini of selected nematode proteins for PTS1 function substantiated predictions made regarding the proteins' peroxisomal location. It is concluded that the eukaryotic PEX5-dependent route for importing PTS1-containing proteins into peroxisomes is conserved in nematodes. C. elegans might emerge as an attractive model system for studying the importance of peroxisomes and affiliated processes in neurodegeneration, and also for studying a beta-oxidation process that is potentially compartmentalized in both mitochondria and peroxisomes.

L5 ANSWER 7 OF 29 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 2000:148069 BIOSIS
DOCUMENT NUMBER: PREV200000148069
TITLE: Neuronal migratory delay in the Zellweger (PEX2) transgenic mouse.
AUTHOR(S): Bamford, N. S. (1); Faust, P. L.
CORPORATE SOURCE: (1) Dept. of Neurology, Columbia University, New York, NY, 10032 USA
SOURCE: Society for Neuroscience Abstracts., (1999) Vol. 25, No. 1-2, pp. 2036.
Meeting Info.: 29th Annual Meeting of the Society for Neuroscience. Miami Beach, Florida, USA October 23-28, 1999 Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L5 ANSWER 8 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999315722 EMBASE
TITLE: Isolation, characterization and mutation analysis of PEX13-defective Chinese hamster ovary cell mutants.
AUTHOR: Toyama R.; Mukai S.; Itagaki A.; Tamura S.; Shimozawa N.; Suzuki Y.; Kondo N.; Wanders R.J.A.; Fujiki Y.
CORPORATE SOURCE: Y. Fujiki, Department of Biology, Kyushu Univ. Graduate School Science, 6-10-1 Hakozaki, Higashi-ku, Fukuoka 812-5581, Japan. yfujiscb@mbox.nc.kyushu-u.ac.jp
SOURCE: Human Molecular Genetics, (1999) 8/9 (1673-1681).
Refs: 37

ISSN: 0964-6906 CODEN: HMGEE5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We isolated peroxisome biogenesis mutants ZP128 and ZP150 from rat PEX2-transformed Chinese hamster ovary (CHO) cells, by the 9-(1'-pyrene)nonanol/ultraviolet method. The mutants lacked morphologically recognizable peroxisomes and showed a typical peroxisome assembly-defective phenotype such as a high sensitivity to 12-(1'-pyrene)dodecanoic acid/UV treatment. By means of **PEX** cDNA transfection and cell fusion, ZP128 and ZP150 were found to belong to a recently identified complementation group H. Expression of human PEX13 cDNA restored peroxisome assembly in ZP128 and ZP150. CHO cell PEX13 was isolated; its deduced sequence comprises 405 amino acids with 93% identity to human Pex13p. Mutation in PEX13 of mutant ZP150 was determined by RT-PCR: G to A transition resulted in one amino acid substitution, Ser319Asn, in one allele and truncation of a 42 amino acid sequence from Asp265 to Lys306 in another allele. Therefore, ZP128 and ZP150 are CHO cell lines with a phenotype of impaired PEX13.

L5 ANSWER 9 OF 29 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 2000:62521 BIOSIS
DOCUMENT NUMBER: PREV200000062521
TITLE: Peroxisomal disorders.
AUTHOR(S): Raymond, Gerald V. (1)
CORPORATE SOURCE: (1) Kennedy Krieger Institute, 707 N Broadway, Baltimore, MD USA
SOURCE: Current Opinion in Pediatrics, (Dec., 1999) Vol. 11, No. 6, pp. 572-576.
ISSN: 1040-8703.
DOCUMENT TYPE: Article
LANGUAGE: English

L5 ANSWER 10 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 2
ACCESSION NUMBER: 1998194311 EMBASE
TITLE: Cloning of human **PEX** cDNA: Expression, subcellular localization, and endopeptidase activity.
AUTHOR: Lipman M.L.; Panda D.; Bennett H.P.J.; Henderson J.E.; Shane E.; Shen Y.; Goltzman D.; Karaplis A.C.
CORPORATE SOURCE: A.C. Karaplis, Div. of Endocrinology, Sir M.B. Davis-Jewish Gen. Hospital, McGill University, 3755 Cote Ste-Catherine Rd., Montreal, Que. H3T 1E2, Canada.
akarapli@ldi.jgh.mccgill.ca
SOURCE: Journal of Biological Chemistry, (29 May 1998) 273/22 (13729-13737).
Refs: 35
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Mutations in the **PEX** gene are responsible for X-linked hypophosphatemic rickets. To gain insight into the role of **PEX** in normal physiology we have cloned the human full-length cDNA and studied its tissue expression, subcellular localization, and peptidase activity. We show that the cDNA encodes a 749-amino acid protein structurally related to a family of neutral endopeptidases that include neprilysin as prototype. By Northern blot analysis, the size of the full-length

PEX transcript is 6.5 kilobases. **PEX** expression, as determined by semiquantitative polymerase chain reaction, is high in bone and in tumor tissue associated with the paraneoplastic syndrome of renal phosphate wasting. **PEX** is glycosylated in the presence of canine microsomal membranes and partitions exclusively in the detergent phase from Triton X-114 extractions of transiently transfected COS cells. Immunofluorescence studies in A293 cells expressing **PEX** tagged with a c-myc epitope show a predominant cell-surface location for the protein with its COOH-terminal domain in the extracellular compartment, substantiating the assumption that **PEX**, like other members of the neutral endopeptidase family, is a type II integral membrane glycoprotein. Cell membranes from cultured COS cells transiently expressing **PEX** efficiently degrade exogenously added **parathyroid hormone**-derived peptides, demonstrating for the first time that recombinant **PEX** can function as an endopeptidase. **PEX** peptidase activity may provide a convenient target for pharmacological intervention in states of altered phosphate homeostasis and in metabolic bone diseases.

L5 ANSWER 11 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 3

ACCESSION NUMBER: 1998385394 EMBASE

TITLE: Genetic screening for X-linked hypophosphatemic mice and ontogenic characterization of the defect in the renal sodium-phosphate transporter.

AUTHOR: Muller Y.L.; Collins J.F.; Ghishan F.K.

CORPORATE SOURCE: Dr. F.K. Ghishan, Department of Pediatrics, Steele Memorial Children's Res. Ctr., Univ. of Arizona Hlth. Sci. Center, 1501 N. Campbell Avenue, Tucson, AZ 85724, United States

SOURCE: Pediatric Research, (1998) 44/5 (633-638).
Refs: 18
ISSN: 0031-3998 CODEN: PEREBL

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
022 Human Genetics
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB X-linked hypophosphatemic (Hyp) rickets is characterized by short stature, rickets, and bone abnormalities. Biochemically, hypophosphatemia and decreased renal reabsorption of phosphate are the hallmark of the disorder. Mutation of the **PEX** gene has been linked to human and murine Hyp rickets. Our study showed that phenotypical changes of this disease could be detected in 6-wk-old mice, but not in 2-wk-old mice. Therefore, we developed a PCR method to identify Hyp mice by detecting a lack of the 3' region of the **PEX** gene. Serum inorganic phosphate (P(i)) levels were decreased, whereas alkaline phosphatase activity was increased in 2- and 6-wk-old Hyp mice. Northern blot showed that renal Na+-P(i) transporter mRNA levels were decreased by 2.1- fold (1.47 .+-. 0.21 densitometric units for normals; 0.68 .+-. 1.43 for Hyp mice; $p < 0.040$) in 2-wk-old Hyp mice and by 1.7-fold (2.41 .+-. 0.42 for normals; 1.44 .+-. 0.33 for Hyp mice; $p < 0.027$) in 6-wk-old mice. Western blot showed that levels of immunoreactive renal Na+-P(i) transporter protein were decreased by 4.5-fold (0.90 .+-. 0.10 for normals; 0.22 .+-. 0.08 for Hyp mice; $p < 0.001$) in 2-wk-old Hyp mice; and by 4.9-fold (1.47 .+-. 0.19 for normals; 0.30 .+-. 0.09 for Hyp mice; $p < 0.0001$) in 6-wk-old Hyp mice. In addition, levels of Na+-P(i) transporter mRNA and protein were increased between 2- and 6-wk-old normal mice, but not in Hyp mice. This study demonstrates an easy assay to detect Hyp mutation and characterizes the defect during ontogeny of the Na+-P(i) transporter in Hyp mice.

L5 ANSWER 12 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 4

ACCESSION NUMBER: 1998086348 EMBASE
TITLE: Spermine deficiency in Gy mice caused by deletion of the spermine synthase gene.
AUTHOR: Lorenz B.; Francis F.; Gempel K.; Bsddrich A.; Josten M.; Schmahl W.; Schmidt J.; Lehrach H.; Meitinger T.; Strom T.M.
CORPORATE SOURCE: T.M. Strom, Abteilung Medizinische Genetik, Kinderpoliklinik, Ludwig-Maximilians-Universitat, Goethestr. 29, 80336 Munchen, Germany. timstrom@pedgen.med.uni-muenchen.de
SOURCE: Human Molecular Genetics, (1998) 7/3 (541-547).
Refs: 34
ISSN: 0964-6906 CODEN: HMGEE5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Two mouse mutations gyro (Gy) and hypophosphatemia (Hyp) are mouse models for X-linked hypophosphatemic rickets and have been shown to be deleted for the 5' and 3' end of the mouse homolog of PHEX(osphate regulating gene with homologies to ndopeptidases on the chromosome; formerly called **PEX**), respectively, In addition to the metabolic disorder observed in Hyp mice, male Gy mice are sterile and show circling behavior and reduced viability. The human SMS (spermine synthase) gene maps .apprx.39 kb upstream of PHEX and is transcribed in the same direction. To elucidate the complex phenotype of Gy mice, we characterized the genomic region upstream of Phex. By establishing the genomic structure of mouse Sms, a 160-190 kb deletion was shown in Gy mice, which includes both Phex and Sms. There are several pseudogenes of SMS/Sms in man and mouse. Northern analysis revealed three different Sms transcripts which are absent in Gy mice. Measurement of polyamine levels revealed a marked decrease in spermine in liver and pancreas of affected male Gy mice. Analysis of brain tissue revealed no gross or histological abnormalities. Gy provides a mouse model for a defect in the polyamine pathway, which is known to play a key role in cell proliferation.

L5 ANSWER 13 OF 29 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 1998:227575 BIOSIS
DOCUMENT NUMBER: PREV199800227575
TITLE: **Pex** mRNA is localized in developing mouse osteoblasts and odontoblasts.
AUTHOR(S): Ruchon, Andrea Frota; Marcinkiewicz, Mieczyslaw; Siefried, Geraldine; Tenenhouse, Harriet S.; Desgroseiller, Luc; Crine, Philippe; Boileau, Guy (1)
CORPORATE SOURCE: (1) Dep. Biochimie, Univ. Montreal, CP 6128, Succ. Centre-Ville, Montreal Qc H3C 3J7 Canada
SOURCE: Journal of Histochemistry and Cytochemistry, (April, 1998) Vol. 46, No. 4, pp. 459-468.
ISSN: 0022-1554.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Mutations in **PEX**, a phosphate-regulating gene with homology to endopeptidase on the X chromosome, were recently identified in patients with X-linked hypophosphatemia (XLH), an inherited disorder of phosphate homeostasis characterized by growth retardation and rachitic and osteomalacic bone disease. To understand the mechanism by which loss of **PEX** function elicits the mutant phenotype, a study of its mRNA localization and ontogenesis was undertaken. Using the reverse transcriptase-nested polymerase chain reaction (RT-nested PCR) with polyA+ RNA purified from mouse testis, a 337-BP **Pex** cDNA fragment was generated and cloned in the pCRII plasmid. The cDNA was used

to generate sense and anti-sense **Pex** riboprobes for in situ hybridization (ISH) and Northern analysis. To survey a large number of different tissues, sagittal sections of embryos and newborn mice were examined. ISH showed the presence of **Pex** mRNA in osteoblasts and odontoblasts. **Pex** gene expression was detectable on Day 15 of embryonic development, which coincides with the beginning of intercellular matrix deposition in bones. Finally, Northern analysis of total RNA from calvariae and teeth of 3-day-old and adult mice showed that the abundance of the 7-KB **Pex** transcript is decreased in adult bones and in nongrowing teeth. The present study demonstrates that **Pex** mRNA is expressed in bones and teeth and suggests that this putative endopeptidase plays an important role in the development of these tissues.

L5 ANSWER 14 OF 29 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 1999:17016 BIOSIS
DOCUMENT NUMBER: PREV199900017016
TITLE: Role of matrix metalloproteinase-2 (MMP-2) and **PEX** , a noncatalytic fragment of MMP-2, in corneal angiogenesis.
AUTHOR(S): Aguilar, E. (1); Gigliotti, B. (1); Bersaglieri, T. (1); Leonard, M. (1); Cheresh, D.; Friedlander, M. (1)
CORPORATE SOURCE: (1) Dep. Cell Biol., Scripps Res. Inst., La Jolla, CA 92037 USA
SOURCE: Molecular Biology of the Cell, (Nov., 1998) Vol. 9, No. SUPPL., pp. 167A.
Meeting Info.: 38th Annual Meeting of the American Society for Cell Biology San Francisco, California, USA December 12-16, 1998 American Society for Cell Biology . ISSN: 1059-1524.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 15 OF 29 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 1998:228230 BIOSIS
DOCUMENT NUMBER: PREV199800228230
TITLE: Molecular analysis of peroxisomal disorders.
AUTHOR(S): Shimozawa, Nobuyuki (1)
CORPORATE SOURCE: (1) Dep. Pediatr., Gifu Univ. Sch. Med., Gifu Japan
SOURCE: No To Hattatsu, (March, 1998) Vol. 30, No. 2, pp. 129-133. ISSN: 0029-0831.
DOCUMENT TYPE: Article
LANGUAGE: Japanese
SUMMARY LANGUAGE: Japanese; English
AB Peroxisome biogenesis disorders (PBD) include Zellweger syndrome (ZS), neonatal adrenoleukodystrophy (NALD) and infantile Refsum disease (IRD). They are classified into ten complementation groups. Five pathogenic genes have been identified using different model systems of peroxisome deficient mutants. PAF-1 and 2 were identified from CHO mutants and were responsible genes for PBD group F and C. Human **PEX** 5, 12 and 1, responsible genes for group 2, 3 and 1, respectively, were cloned by homology search between yeast **PEX** genes and human genes on the cDNA data base. Adrenoleukodystrophy (ALD), the most frequent peroxisomal disorder, shows phenotypic heterogeneity. Its responsible gene was cloned by positional cloning. It encodes a 75 kDa peroxisomal membrane protein (ALDP) that is a member of the ATP-binding cassette transporter family. There are about 120 different mutations including missense, nonsense and splice mutations, as well as insertions and deletions of a few base pairs. There is no correlation between the clinical phenotype and the ALDP gene mutation. Recently, **animal models** have been produced by targeted mutation of the PBD and ALD genes. The mouse model should facilitate researches on PBD and ALD, especially those on regulatory factors of their phenotypic heterogeneity and on new therapeutic approaches.

L5 ANSWER 16 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 5
ACCESSION NUMBER: 1998140989 EMBASE
TITLE: Molecular analysis of peroxisomal disorders.
AUTHOR: Shimozawa N.
CORPORATE SOURCE: Dr. N. Shimozawa, Department of Pediatrics, Gifu University School of Medicine, Gifu, Japan
SOURCE: No To Hattatsu, (1998) 30/2 (128-133).
Refs: 1
ISSN: 0029-0831 CODEN: NTHAA7
COUNTRY: Japan
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
007 Pediatrics and Pediatric Surgery
008 Neurology and Neurosurgery
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: Japanese
SUMMARY LANGUAGE: Japanese; English
AB Peroxisome biogenesis disorders (PBD) include Zellweger syndrome (ZS), neonatal adrenoleukodystrophy (NALD) and infantile Refsum disease (IRD). They are classified into ten complementation groups. Five pathogenic genes have been identified using different model systems of peroxisome deficient mutants. PAF-1 and 2 were identified from CHO mutants and were responsible genes for PBD group F and C. Human **PEX** 5, 12 and 1, responsible genes for group 2, 3 and 1, respectively, were cloned by homology search between yeast **PEX** genes and human genes on the cDNA data base. Adrenoleukodystrophy (ALD), the most frequent peroxisomal disorder, shows phenotypic heterogeneity. Its responsible gene was cloned by positional cloning. It encodes a 75 kDa peroxisomal membrane protein (ALDP) that is a member of the ATP-binding cassette transporter family. There are about 120 different mutations including missense, nonsense and splice mutations, as well as insertions and deletions of a few base pairs. There is no correlation between the clinical phenotype and the ALDP gene mutation. Recently, **animal models** have been produced by targeted mutation of the PBD and ALD genes. The mouse model should facilitate researches on PBD and ALD, especially those on regulatory factors of their phenotypic heterogeneity and on new therapeutic approaches.

L5 ANSWER 17 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 6
ACCESSION NUMBER: 1998148625 EMBASE
TITLE: Cellular/molecular control of renal Na/P(i)-cotransport.
AUTHOR: Murer H.; Forster I.; Hilfiker H.; Pfister M.; Kaissling B.; Lotscher M.; Biber J.
CORPORATE SOURCE: Dr. H. Murer, Institute of Physiology, Switzerland Physiologisches Institut, Winterthurerstrasse 190, CH-8057 Zurich, Switzerland. murer@physiol.unizh.ch
SOURCE: Kidney International, Supplement, (1998) 53/65 (S2-S10).
Refs: 84
ISSN: 0098-6577 CODEN: KISUDF
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 002 Physiology
028 Urology and Nephrology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A type II Na/P(i)-cotransporter located in the brush border membrane is the rate limiting and physiologically regulated step in proximal tubular phosphate (P(i)) reabsorption. In states of altered P(i)-reabsorption [for example, in response to **parathyroid hormone** (**PTH**) and to altered dietary intake of P(i) or as a consequence of genetic abnormabilities], brush border expression of the type II

Na/P(i)-cotransporter is accordingly modified. **PTH** initiates a regulatory cascade leading to membrane retrieval, followed by lysosomal degradation of this transporter; recovery from inhibition requires its de novo synthesis. P(i)-deprivation leads to an increased brush border expression of transporters that does not appear to require de novo synthesis in the short term. P(i)-overload leads to membrane retrieval and degradation of transporters. Finally, in animals with genetically altered P(i)-handling (Hyp; Gy) the brush border membrane expression of the type II Na/P(i)- cotransporter is also reduced, suggesting that a genetically altered protein (such as **PEX** in Hyp) controls the expression of this transporter.

L5 ANSWER 18 OF 29 MEDLINE
ACCESSION NUMBER: 1998212789 MEDLINE
DOCUMENT NUMBER: 98212789 PubMed ID: 9551425
TITLE: Cellular/molecular control of renal Na/Pi-cotransport.
AUTHOR: Murer H; Forster I; Hilfiker H; Pfister M; Kaissling B; Lotscher M; Biber J
CORPORATE SOURCE: Institute of Physiology, Switzerland Physiologisches Institut, Zurich, Switzerland.. murer@physiol.unizh.ch
SOURCE: KIDNEY INTERNATIONAL. SUPPLEMENT, (1998 Apr) 65 S2-10. Ref: 84
Journal code: KVC; 7508622. ISSN: 0098-6577.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980529
Last Updated on STN: 19980529
Entered Medline: 19980521

AB A type II Na/Pi-cotransporter located in the brush border membrane is the rate limiting and physiologically regulated step in proximal tubular phosphate (Pi) reabsorption. In states of altered Pi-reabsorption [for example, in response to **parathyroid hormone** (**PTH**) and to altered dietary intake of Pi or as a consequence of genetic abnormalities], brush border expression of the type II Na/Pi-cotransporter is accordingly modified. **PTH** initiates a regulatory cascade leading to membrane retrieval, followed by lysosomal degradation of this transporter; recovery from inhibition requires its de novo synthesis. Pi-deprivation leads to an increased brush border expression of transporters that does not appear to require de novo synthesis in the short term. Pi-overload leads to membrane retrieval and degradation of transporters. Finally, in animals with genetically altered Pi-handling (Hyp; Gy) the brush border membrane expression of the type II Na/Pi-cotransporter is also reduced, suggesting that a genetically altered protein (such as **PEX** in Hyp) controls the expression of this transporter.

L5 ANSWER 19 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97099288 EMBASE
DOCUMENT NUMBER: 1997099288
TITLE: **Pex/PEX** tissue distribution and evidence for a deletion in the 3' region of the **Pex** gene in X-linked hypophosphatemic mice.
AUTHOR: Beck L.; Soumounou Y.; Martel J.; Krishnamurthy G.; Gauthier C.; Goodyer C.G.; Tenenhouse H.S.
CORPORATE SOURCE: H.S. Tenenhouse, Montreal Children's Hospital, 2300 Tupper Street, Montreal, Que. H3H 1P3, United States. mdht@musica.mcgill.ca

SOURCE: Journal of Clinical Investigation, (1997) 99/6 (1200-1209).
Refs: 40
ISSN: 0021-9738 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
033 Orthopedic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **PEX**, a phosphate-regulating gene with homology to endopeptidases on the X chromosome, was recently identified as the candidate gene for X-linked hypophosphatemia. In the present study, we cloned mouse and human **Pex/PEX** cDNAs encoding part of the 5' untranslated region, the protein coding region, and the entire 3' untranslated region, determined the tissue distribution of **Pex/PEX** mRNA, and characterized the **Pex** mutation in the murine Hyp homologue of the human disease. Using the reverse transcriptase/polymerase chain reaction (RT/PCR) and ribonuclease protection assays, we found that **Pex/PEX** mRNA is expressed predominantly in human fetal and adult mouse calvaria and long bone. With RNA from Hyp mouse bone, an RT/PCR product was generated with 5' but not 3' **Pex** primer pairs and a protected **Pex** mRNA fragment was detected with 5' but not 3' **Pex** ribo-probes by ribonuclease protection assay. Analysis of the RT/PCR product derived from Hyp bone RNA revealed an aberrant **Pex** transcript with retention of intron sequence downstream from nucleotide 1302 of the **Pex** cDNA. **Pex** mRNA was not detected on Northern blots of poly (A)+ RNA from Hyp bone, while a low-abundance **Pex** transcript of .simeq. 7 kb was apparent in normal bone. Southern analysis of genomic DNA from Hyp mice revealed the absence of hybridizing bands with cDNA probes from the 3' region of the **Pex** cDNA. We conclude that **Pex/PEX** is a low-abundance transcript that is expressed predominantly in bone of mice and humans and that a large deletion in the 3' region of the **Pex** gene is present in the murine Hyp homologue of X-linked hypophosphatemia.

L5 ANSWER 20 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 7
ACCESSION NUMBER: 1998032157 EMBASE
TITLE: Oncogenic osteomalacia: Is there a new phosphate regulating hormone?.
AUTHOR: Nelson A.E.; Robinson B.G.; Mason R.S.
CORPORATE SOURCE: Dr. A.E. Nelson, Molecular Genetics Department, Kolling Inst. of Medical Research, Royal North Shore Hospital, St Leonards, NSW 2065, Australia. annen@med.usyd.edu.au
SOURCE: Clinical Endocrinology, (1997) 47/6 (635-642).
Refs: 68
ISSN: 0300-0664 CODEN: CLENAO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Oncogenic osteomalacia is a syndrome associated with rare, usually mesenchymal tumours, which is characterized by hypophosphataemia, phosphaturia and low concentrations of 1,25-dihydroxyvitamin D. The reversal of clinical and biochemical abnormalities following removal of the tumour, indicates it is the source of a humoral factor that is responsible for these abnormalities. It has been demonstrated that the humoral factor inhibits renal phosphate uptake and reduces 1,25-dihydroxyvitamin D production. Although there is evidence that it may act via **parathyroid hormone/parathyroid hormone**-related peptide receptors and may be a peptide, the factor has not yet been identified, nor has its relationship to factors involved

in X-linked hypophosphataemic rickets been established. We propose unifying hypotheses for the pathogenesis of oncogenic osteomalacia and X-linked hypophosphataemic rickets which involve defects in the **PEX** gene. These hypotheses do not fully explain all the available data and it remains possible that hormone(s) with little or no role in X-linked hypophosphataemic rickets may be responsible for oncogenic osteomalacia.

L5 ANSWER 21 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 8
ACCESSION NUMBER: 97346024 EMBASE
DOCUMENT NUMBER: 1997346024
TITLE: Positional cloning of the **PEX** gene: New insights into the pathophysiology of X-linked hypophosphatemic rickets.
AUTHOR: Econs M.J.; Francis F.
CORPORATE SOURCE: M.J. Econs, Dept. of Medicine, Indiana University Medical Center, 975 W. Walnut St., Indianapolis, IN 46202, United States
SOURCE: American Journal of Physiology - Renal Physiology, (1997) 273/4 42-4 (F489-F498).
Refs: 90
ISSN: 0363-6127 CODEN: AJPPFK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
033 Orthopedic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB X-linked hypophosphatemic rickets (HYP) is the most common form of hereditary renal phosphate wasting. The hallmarks of this disease are isolated renal phosphate wasting with inappropriately normal calcitriol concentrations and a mineralization defect in bone. Studies in the Hyp mouse, one of the murine models of the human disease, suggest that there is an .apprx.50% decrease in both message and protein of NPT-2, the predominant sodium-phosphate cotransporter in the proximal tubule. However, human NPT-2 maps to chromosome 5q35, indicating that it is not the disease gene. Positional cloning studies have led to the identification of a gene, **PEX**, which is responsible for the disorder. Further studies have led to identification of the murine **Pex** gene, which is mutated in the murine models of the disorder. These studies, in concert with other studies, have led to improved understanding of the pathophysiology of HYP and a new appreciation for the complexity of normal phosphate homeostasis.

L5 ANSWER 22 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97132353 EMBASE
DOCUMENT NUMBER: 1997132353
TITLE: New perspectives on the biology and treatment of X-linked hypophosphatemic rickets.
AUTHOR: Carpenter T.O.
CORPORATE SOURCE: Dr. T.O. Carpenter, Department of Pediatrics, Yale University School of Medicine, New Haven, CT 06520-8064, United States
SOURCE: Pediatric Clinics of North America, (1997) 44/2 (443-466).
Refs: 109
ISSN: 0031-3955 CODEN: PCNAA8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The recently established findings that should be recognized in a

mechanistic explanation of pathophysiology in XLH/Hyp include the following: Human and murine studies suggest that a humoral factor mediates the defect in renal phosphate transport. Many tumors that produce such a factor are of primitive mesenchymal origin and are not infrequently found in bone. The disease of mineralized tissues (bones and teeth) seem to be independent of disease expression at the kidney (as reflected by circulating phosphate levels). Mineralized tissues may reflect a gene dose effect, which does not seem to be present in kidney. Production of 1,25(OH)2D is not appropriate for the ambient hypophosphatemia. The mutated gene in XLH seems to encode an endopeptidase, and although expressed abundantly in murine bone relative to other tissues, it is underexpressed in Hyp mice. Renal intracellular P is probably normal, which may mask the hypophosphatemic stimulus to renal 1,25(OH)2D production. A unifying hypothesis that incorporates these findings is as follows: A putative Pi-regulating substance may be secreted by bone cells (as in OHO tumors). The author postulates that in normal steady state times of Pi sufficiency, elicitation of such a factor may preserve intracellular Pi at the proximal renal tubular cell. Luminal membrane Pi transport and 1.alpha.-hydroxylation of vitamin D would therefore be normally maintained. During Pi insufficiency, a decrease in the factor would decrease intracellular Pi, thereby mediating an increase in luminal membrane transport of Pi and 1.alpha.-hydroxylation of vitamin D. Unregulated persistence of such a factor during brief Pi deprivation would disrupt appropriate renal Pi conservation and generation of 1,25(OH)2D, the precise renal defects seen in XLH/Hyp. The author suggests that the synthesis, processing, or secretion of this putative humoral factor is rendered abnormal in XLH by mutations in the **PEX** gene, such that normal regulation of the Pi homeostatic system is disrupted. Further levels of complexity may exist: the renal- active factor may act directly on bone cells in an autocrine or paracrine fashion, or inappropriate regulation of intracellular Pi at the parathyroid cell may occur, resulting in the tendency to hypersecretion of **PTH**. Such a system would provide a mechanism by which skeletal mineral demands can be regulated at the renal level. Although this would be of physiologic service to the organism, no such system has been clearly established. This speculative hypothesis is summarized in Figure 5. Finally, others have suggested that a humoral factor interacts with receptors on the luminal membrane of renal tubular cells, increasing protein kinase C activity, which in turn results in the described renal tubular defects.

L5 ANSWER 23 OF 29 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 1998:111903 BIOSIS
DOCUMENT NUMBER: PREV199800111903
TITLE: Spermine deficiency in Gy mice caused by deletion of the spermine synthase genes.
AUTHOR(S): Lorenz, B. (1); Francis, F.; Gempel, K.; Boeddrich, A.; Josten, M.; Schmahl, W.; Gerbitz, K. D.; Lehrach, H.; Meitinger, T. (1); Strom, T. M. (1)
CORPORATE SOURCE: (1) Abteilung Medizinische Genetik, Ludwig-Maximillians-Univ., Muenchen Germany
SOURCE: American Journal of Human Genetics, (Oct., 1997) Vol. 61, No. 4 SUPPL., pp. A338.
Meeting Info.: 47th Annual Meeting of the American Society of Human Genetics Baltimore, Maryland, USA October 28-November 1, 1997
ISSN: 0002-9297.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 24 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 9
ACCESSION NUMBER: 97054291 EMBASE
DOCUMENT NUMBER: 1997054291

TITLE: Per gene deletions in Gy and Hyp mice provide mouse models for X-linked hypophosphatemia.
AUTHOR: Strom T.M.; Francis F.; Lorenz B.; Boddrich A.; Econs M.J.; Lehrach H.; Meitinger T.
CORPORATE SOURCE: T.M. Strom, Abteilung Medizinische Genetik, Kinderpoliklinik, Ludwig-Maximilians-Universitat, Goethestr 29, 80336 Munchen, Germany
SOURCE: Human Molecular Genetics, (1997) 6/2 (165-171).
Refs: 34
ISSN: 0964-6906 CODEN: HMGEE5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB X-linked hypophosphatemic rickets in humans is caused by mutations in the **PEX** gene which codes for a protein homologous to neutral endopeptidases. Hyp and Gy mice both have X-linked hypophosphatemic rickets, although genetic data and the different phenotypic spectra observed have previously suggested that two different genes are mutated. In addition to the metabolic disorder observed in Hyp mice, male Gy mice are sterile and show circling behavior and reduced viability. We now report the cloning of the mouse homolog of **PEX** which is highly conserved between man and mouse. The 3' end of this gene is deleted in Hyp mice. In Gy mice, the first three exons and the promotor region are deleted. Thus, Hyp and Gy are allelic mutations and both provide mouse models for X-linked hypophosphatemia.

L5 ANSWER 25 OF 29 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 1996:500493 BIOSIS
DOCUMENT NUMBER: PREV199699222849
TITLE: Recently clones genes involved in calcium and phosphate homeostasis.
AUTHOR(S): Strom, Tim M. (1); Francis, Fiona
CORPORATE SOURCE: (1) Abt. Paediatrische Genetik, Kinderpoliklinik, Ludwig-Maximilians-Univ., Goethestr. 29, 80336 Muenchen Germany
SOURCE: Schoenau, E. [Editor]. International Congress Series, (1996) No. 1105, pp. 53-58. International Congress Series; Paediatric osteology: New developments in diagnostics and therapy.
Publisher: Elsevier Science Publishers B.V. PO Box 211, Sara Burgerhartstraat 25, 1000 AE Amsterdam, Netherlands.
Meeting Info.: First International Workshop on Paediatric Osteology Cologne, Germany October 5-7, 1995
ISSN: 0531-5131. ISBN: 0-444-82277-1.
DOCUMENT TYPE: Book; Conference
LANGUAGE: English

L5 ANSWER 26 OF 29 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 1996:497912 BIOSIS
DOCUMENT NUMBER: PREV199699220268
TITLE: Hypophosphatemic rickets: Mutation screening in the **PEX** gene and cloning of the mouse homolog.
AUTHOR(S): Strom, T. M. (1); Francis, F.; Lorenz, B. (1); Boeddrich, A.; Cagnoli, M.; Mohnike, K. L.; Lehrach, H.; Meitinger, T. (1); (germany), Hyp Consortium
CORPORATE SOURCE: (1) Abt. Paediatrische Genetik, Kinderpoliklinik LMU, Muenchen Germany
SOURCE: Hormone Research (Basel), (1996) Vol. 46, No. SUPPL. 2, pp. 84.

Meeting Info.: 35th Annual Meeting of the European Society for Paediatric Endocrinology Montpellier, France September 15-18, 1996
ISSN: 0301-0163.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 27 OF 29 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 1996:355236 BIOSIS
DOCUMENT NUMBER: PREV199699077592
TITLE: The mouse homolog of **PEX** is deleted in Gy mice.
AUTHOR(S): Strom, Tim M. (1); Francis, F.; Econs, M. J.; Lorenz, B. (1); Meindl, A. (1); Rowe, P. S. N.; O'Riordan, J. L. H.; Oudet, C.; Drezner, M. K.; Lehrach, H.; Meitinger, T. (1)
CORPORATE SOURCE: (1) Abt. Paediatr. Genet., Kinderpoliklin., LMU Muenchen, Goethestr. 29, 80336 Muenchen Germany
SOURCE: European Journal of Human Genetics, (1996) Vol. 4, No. SUPPL. 1, pp. 1.
Meeting Info.: 28th Annual Meeting of the European Society of Human Genetics London, England, UK April 11-13, 1996
ISSN: 1018-4813.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 28 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 10
ACCESSION NUMBER: 94135864 EMBASE
DOCUMENT NUMBER: 1994135864
TITLE: Production of human **parathyroid hormone** by recombinant Escherichia coli TG1 on synthetic medium.
AUTHOR: Harder M.P.F.; Sanders E.A.; Wingender E.; Deckwer W.-D.
CORPORATE SOURCE: GBF, Gesellsch. fur Biotechn. Forsch. mbH, Mascheroder Weg 1,D-38124 Braunschweig, Germany
SOURCE: Journal of Biotechnology, (1994) 32/2 (157-164).
ISSN: 0168-1656 CODEN: JBITD4
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Production of human **parathyroid hormone** (hPTH) by Escherichia coli TG1:I52cIts was studied. The hPTH is expressed as a fusion protein under control of the bacteriophage .lambda.p(R) promoter. The organism grows on glucose/mineral salt medium and the expression of the gene product was investigated under variation of temperature and growth rate prior to and after induction. hPTH formation largely depends on cultivation temperature and is optimal for a temperature shift from 30 to 38.degree.C. Product expression is growth coupled and specific hPTH concentration is independent of growth rate. The results are compared with a previous study on E. coli N4830:**pEX**-PPTH grown on complex media.

L5 ANSWER 29 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 11
ACCESSION NUMBER: 93167197 EMBASE
DOCUMENT NUMBER: 1993167197
TITLE: Studies on the production of human **parathyroid hormone** by recombinant Escherichia coli.
AUTHOR: Harder M.P.F.; Sanders E.A.; Wingender E.; Deckwer W.-D.
CORPORATE SOURCE: GBF/Gessels. Biotechn. Forchung mbH, Biochemical Engineering, Mascheroder Weg 1,W-3300 Braunschweig, Germany
SOURCE: Applied Microbiology and Biotechnology, (1993) 39/3

(329-334).
ISSN: 0175-7598 CODEN: AMBIDG
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Expression of human **parathyroid hormone**, hPTH(1-84), by escherichia coli N4830:**pEX**-PPTH was studied in controlled bioreactors. The hPTH is expressed as a fusion protein under control of the bacteriophage .lambda.p(R) promoter. In batch runs, low biomass concentrations but high specific hPTH productivities were obtained with complex TY (bactotryptone and yeast extract) medium whereas high biomass concentration and low specific productivities were found when fructose was used instead of bactotryptone (YF medium). The preinduction temperature was always 30.degree. C; the temperature shift to induce production of fusion protein was varied from 36 to 42.degree.C. Formation of hPTH passed a pronounced maximum as a function of induction temperature when using YF medium. However, the optimum temperature shift was 38.degree.C for both media used. For this temperature increase both media yielded about the same volumetric hPTH productivity (approx. 30 mg hPTH/l per hour). By applying a fed-batch strategy for the YF medium, the productivity of the recombinant protein could be further increased mor than fourfold. Compared to shake-flask experiments, the hPTH yield could be increased by a factor larger than 20.

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